SCIPOD

USING MACHINE LEARNING TO PREDICT BACTERIAL GROWTH ACCORDING TO THE MEDIA COMPONENTS

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Using Machine Learning to Predict Bacterial Growth According to the Media Components

Bacterial growth depends on the complex interactions of a multitude of chemical components. Microbiologists have long attempted to predict bacterial growth according to culture media components, and have employed a variety of mathematical and computational models to this end. Dr Bei-Wen Ying and her colleagues at the University of Tsukuba, Japan, successfully applied machine learning to understand the contribution of media culture components to bacterial growth. Their work makes a significant contribution to growth prediction and demonstrates that machine learning can be employed in the exploration of the complex dynamics that regulate living systems.

Bacterial growth is one of the foundational phenomena in microbiology. Despite the large body of research already conducted to shed light on the regulatory mechanisms behind bacterial growth, growth dynamics remain difficult to predict.

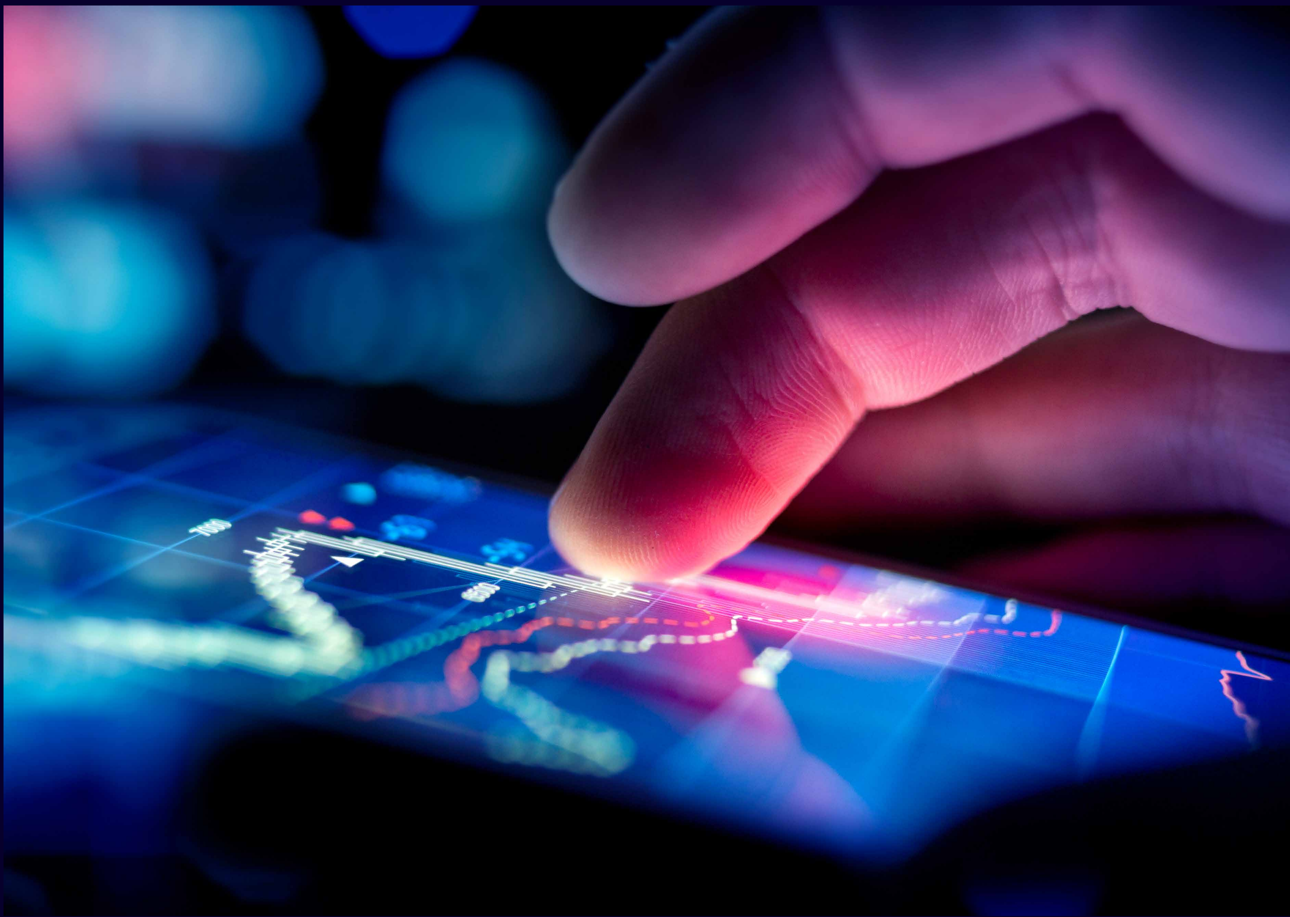
Bacterial growth is determined by a multitude of chemicals and biomolecules and how they interact in both the internal and external environment of the cell. The contribution of single components of the feeding medium to the overall growth dynamics is not clear.

Since growth prediction in certain culture conditions involves the input of a large number of patterns, it can be analysed through a combination of high-throughput experimental techniques and the aid of data science. Machine learning allows us to model the growth in a chemical landscape where millions of biochemical reactions can occur simultaneously within a single cell. Machine learning has already made invaluable contributions to many fields across the life sciences, including genetics and cellular imaging.

Dr Bei-Wen Ying and her colleagues at the University of Tsukuba, Japan, first collected a big data set using high throughput growth assays, and then employed a machine learning approach to predict if – and then how – the media components contribute to bacterial growth.

In 2019, the Ying group published addressing the contribution of the chemical components in the media to the key parameters of bacterial growth. One is growth rate, which represents how fast the bacterial cells grow. The other is saturated density, which represents how large the final population size is.

The study investigated how the population growth of asexual populations could be explained by the chemical components of the medium, combining for the first time a high-throughput growth assay with the machine learning algorithms. The high-throughput



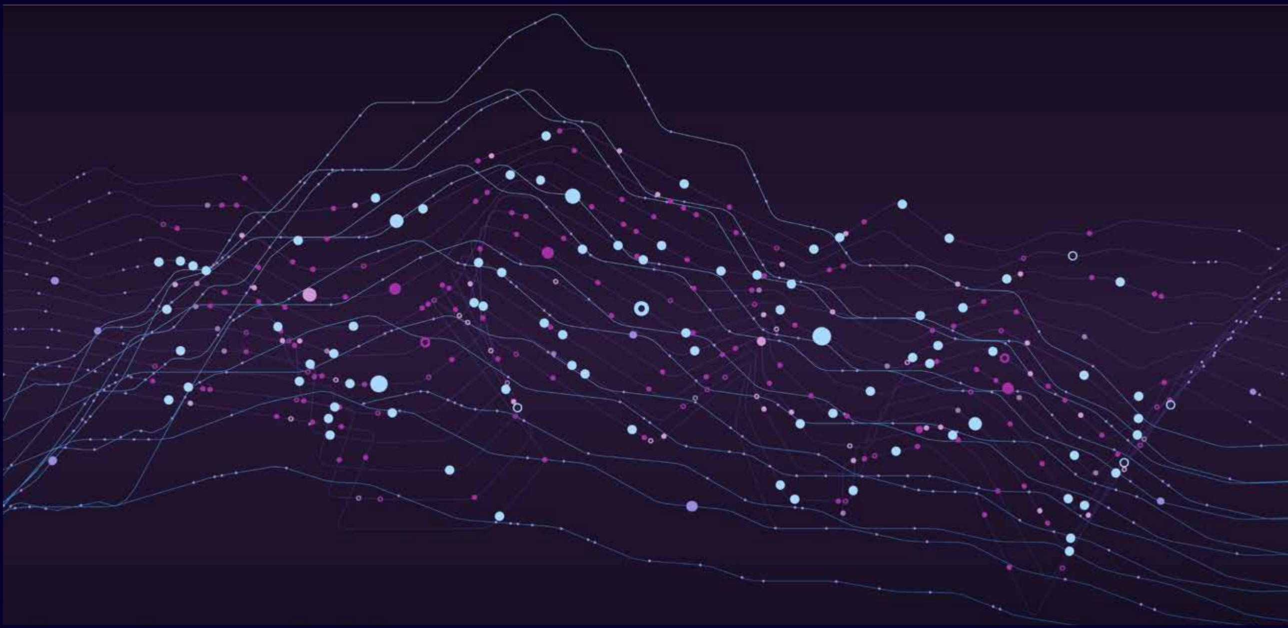
growth assays, the variation of chemical compositions and the data processing methods were all fine-tuned to achieve reliable and highly precise data set.

Dr Ying and her colleagues chose E. coli cells for their bacterial growth studies. They used the fundamental chemical compounds routinely used for bacterial growth, including carbon, ammonium, metal ions, vitamins and amino acids. They generated a growth landscape that was as broad as possible, using chemical concentrations that were out of the ranges generally used in laboratories. To maintain a constant pH, they employed a phosphate buffer with the same concentration in all the combinations.

The number of data analysed in the study was impressive, considering it was the first attempt in the field. A total of 1,336 temporal growth records corresponding to 225 different media composed of 13 chemical components, were generated. Big data sets linking the growth parameters to the chemical combinations were subjected to decision tree learning; this allowed the researchers to identify the factors that influence decision making in the growth among the 13 chemicals.

Dr Ying and her colleagues found that among the 13 chemical components under investigation, the ammonium ion affected the growth rate most significantly. Four chemical components, magnesium, sulfate, and chloride ions, as well as glucose, appeared in the decision tree. They further found that when both ammonium and magnesium ions were out of their optimal ranges, an excess amount of ammonium or the depletion of magnesium would cause zero growth.

This finding led Dr Ying to conclude that it was the nitrogen source but not the carbon source that presented the highest priority in deciding the growth rate of the bacterial strain tested. She predicted that three chemical components – ammonium, magnesium and glucose – are common decision-makers for both the growth rate and the saturated density. The predicted optimal concentrations for either fast growth or high density were identical in glucose, but they were different for ammonium and magnesium. Dr Ying believes that these novel findings could not be achieved when applying routine microbiological experiments or mathematical modelling.



To verify the different mechanisms observed for the first time by the machine learning approach, an experimental examination of ammonium and glucose were performed by Dr Ying's collaborators. The ammonium and glucose concentrations in the experiment were approximately 63.2 and 22.4 milli-molar. The higher than usual ammonium concentration resulted in an increased growth rate and a lower saturated density, which is the cell density at which further cell growth ceases. Changes in the glucose concentration, on the other hand, led to changes in the growth rate and the saturated density in the same direction

Dr Ying's study was the first reported attempt to introduce machine learning into the growth analysis of bacterial cultures. The study presented the successful application of decision tree learning to evaluate the contributions of chemical components to bacterial growth. The approach prevented bias from the investigator's knowledge of the scientific literature or personal expertise in the field, so innovative findings on bacterial growth could be obtained.

The most intriguing finding of the study was that the ammonium ions served as the top-level decision-maker for bacterial growth and determined the growth maximum. The nitrogen in the ammonium ions was an essential chemical element for the biosynthesis of nucleotides, the building blocks of DNA and RNA.

Similarly, magnesium was the common factor in the growth rate and the saturated density. It was not surprising that the bacterial growth required magnesium, as it is a cofactor required in the enzymatic reactions within cells.

Another intriguing finding was the secondary priority of glucose in determining bacterial growth. Taken together these findings could be considered in the synthesis and metabolic design of biological systems.

Although the findings provide valuable hints for further studies on bacterial growth, the tested chemical components in the study were only limited to 13, a sample size that may not be large enough to fully comprehend the chemical contributions to bacterial growth.

Future studies connecting the big data of the cell growth dynamics to machine learning algorithms will be needed to further understand the fundamental principles of complex living systems. The study nonetheless confirms the essential contribution that machine learning offers for future developments in the life sciences.

This SciPod is a summary of the paper: 'Predicting the decision-making chemicals used for bacterial growth' published in Nature Scientific Reports. DOI: https://doi.org/10.1038/s41598-019-43587-8

For further information, you can visit http://www.u.tsukuba.ac.jp/~ying.beiwen.gf/en/index.html or connect with Dr Ying at ying.beiwen.gf@u.tsukuba.ac.jp